RESEARCH PAPER

"In silico screening of bioactive compounds derived from Moringa oleifera Against SARS-CoV-2"

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Abstract:-

The World Health Organization recorded 323,610,370 COVID-19 cases, with 5,529,693 fatalities. SARS-CoV-2 is one of seven coronaviruses known to cause severe lower respiratory tract dysfunction. One of the most well-known and widely disseminated plant species is Moringa oleifera Lam. (Moringaceae family). The World Health Organization recorded 323,610,370 COVID-19 cases, with 5,529,693 fatalities. SARS-CoV-2 is one of seven coronaviruses known to cause severe lower respiratory tract dysfunction. One of the most well-known and widely disseminated plant species is Moringa oleifera Lam. (Moringaceae family). The 3D crystallographic structure of the COVID19 receptor (PDB ID-6M71, 6VYO, 6VYB, and 6Y2F) was obtained from the Protein Data Bank and utilized as a protein target for in-silico experiments. Molecular docking was performed using Auto Dock 4 and AutoDock Vina. A blind docking approach was employed to encompass all possible ligand binding sites. The binding free energy (kcal/mol) was utilized to calculate the binding affinity. This study reveals that M. oleifera, a polyphenolic compound, may possess antiviral activity against the COVID19 receptor responsible for SARS-CoV-2 disease, as predicted in silico. Molecular docking data suggests that Anthraquinone (-7.4, -7.8, -7.7,-8.3 Kcal/mol.) and Sitogluside(-7.4, -7.1, -8.4,-7.3 Kcal/mol) have greater activity than Serpentine (-7.2, -7.6, -6.8,-7.5 Kcal/mol). They have good binding energy. & they are good energy booster in covid 19 disease.

Keywords:- Anthraquinone, sitogluside,serprntine, Moringa oleifera, COVID19

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Introduction:-

COVID-19 is a worldwide illness that emerged near the end of 2019. In January 2022, the World Health Organisation reported 323,610,370 cases of COVID-19, resulting in 5,529,693 deaths.1 SARS-CoV-2 is one of seven coronaviruses that can cause severe lower respiratory tract dysfunction.2 The virus spreads through the innate immune response in humans by binding to the major receptor, ACE2. This illness targets respiratory congenital problems, including hypertension, malignant tumours, chronic obstructive lung disease, coronary heart disease, and chronic renal disease, which can be harmful. For senior patients with comorbidities, this can be fatal. In 145 instances with comorbidities, 51 patients died.

One of the most well-known and widely spread plant species is Moringa oleifera Lam. (Moringaceae family)[1]. Many names for Moringa exist around the world, such as "benzolive tree, horseradish tree, drumstick tree, mulangay, moonga, saijhan, marango, sajna, mlonge, or Ben oil tree." The moringa tree is also known as a "miracle tree" [2], because it has significant socioeconomic value. It contains important pharmaceutical, industrial, and extreme nutritional components. It is well known that secondary metabolites contribute significantly in the therapeutic application of plant species in traditional healing system [3].

Crotenoids, alkaloid, flavonoid, glycoside, anthocyanin, anthraquinone, saponins, tannins, steroids, and terpenoids are all abundant in different sections of M. oleifera[4]. These phytochemicals have a major role in preventing a number of illnesses, including diabetes ,covid-19, cancer, heart disease, age-related functional problems, arthritis, and inflammation.

The Moringa oleifera plant is native to the Himalayan foothills of northern India and is widely dispersed across the Pacific Islands, Asia, and Africa. The horseradish tree and drumstick tree are two frequent names for it, and it is also known as "tropical natural nutrition." The plant's leaves, seeds, fruit pods, and roots all contain important nutritional and medicinal components . Several components of this versatile tree have been shown to exhibit pharmacological qualities such as antioxidant, anti-inflammatory, anti-microbial, anti-fibrotic, anti-hyperglycemic, and anti-tumor activity .

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Because of its significant nutritional value, Moringa oleifera leaves have highly essential therapeutic and medical qualities . Moringa oleifera's high and unique immunological perspective inspires a concept to investigate its antiviral activity against COVID-19 sickness[5] [6] [7] [8]. Moringa oleifera, Lam. leaves were collected for phytochemical analysis using the gas chromatography-mass spectroscopy (GC-MS) method. Approximately thirty-seven phytochemicals from the phytosterols, polyphenols, terpenes, fatty acids, and aliphatic hydrocarbon families were discovered. To investigate potential hits against SARS-CoV-2, these phytochemicals were assessed utilizing in silico molecular docking, toxicity potential, and drug-likeness prediction. The top sixteen hits of Moringa oleifera components have a strong affinity for the SARS-CoV-2 spike glycoprotein and spike RBD-ACE2 protein. The β-tocopherol-spike glycoprotein and β-sitosterol-spike RBD-ACE2 complexes were the most stable and compact over the 100-ns simulation, indicating strong binding interactions. The top sixteen phytoconstituents, including β-tocopherol and β-sitosterol, have drug-like properties with no predicted toxicity. Further optimization through in vitro and clinical investigations is necessary for drug development[9].

Table 1:- Plant parts & the medicinal uses of Moringa oleifera with its references.

Sr.no	Plant part	Medicinal use	Reference
1	Stembark	Cure eye diseases, tuberculosis, Cancer tumors and to heal ulcers, Covid 19	SiddhurajuandBecker, 2003;Anwaretal.,2007[10].
2	Flower	Stimulant ,Cancer tumors, spleen enlargement; lowers VLDL, LDL cholesterol ,Covid 19 .	SiddhurajuandBecker, 2003;Mehtaetal., 2003;Anwaretal.,2007[11].

Material and methods :-

1)Derivatives:-

One of the most well-known and widely spread plant species is Moringa oleifera Lam. (Moringaceae family) (Anwar et al., 2007).

Many names for Moringa exist around the world, such as "benzolive tree, horseradish tree, drumstick tree, mulangay, moonga, saijhan, marango, sajna, mlonge, or Ben oil tree." The moringa tree is also known as a "miracle tree" , because it has significant socioeconomic value. It contains important pharmaceutical, industrial, and extreme nutritional components.This study selected Anthraquinone , sitogluside , serpentine as three derivatives . the structure of these derivatives as 3D conformers in SDF format were received from the PubChem Database , also called the Library of Drug Molecule[12] .

Phytochemicals in M. oleifera, including anthraquinone, , serpentine, sitogluside were isolated and analysed using PubChem. Pub Chem pro provides open access to knowledge about chemical compounds and their biological roles. The Substance database contains chemical information provided by individual data contributors to PubChem, whereas the compound database includes unique chemical structures retrieved from the Substance database[13].

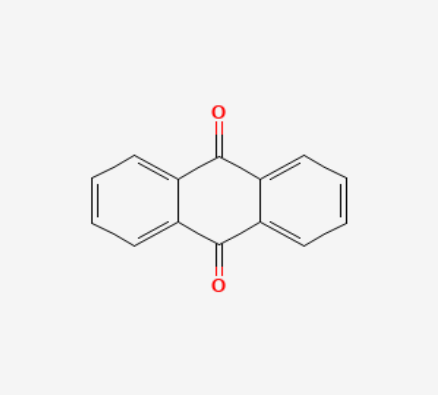

Figure 1:- Anthraquinone

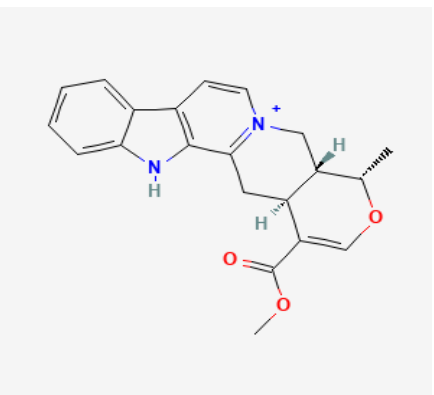

Figure 2:- Serpentine

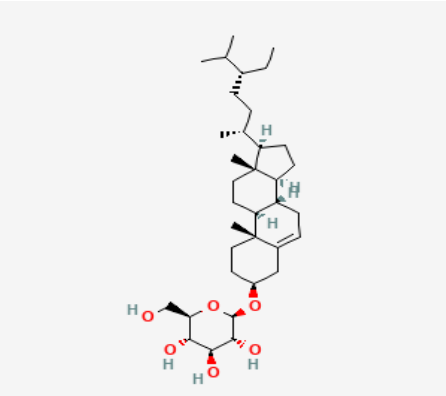

Figure 3:- Sitogluside

2)Protein Preparation:-

3D crystaloghraphic structure of COVID receptors (PDB ID- 6M71, 6VYO, 6VYB, 6Y2F) were received from Protein Data Bank and used as protein target for in-silico studies . subsequently , the protein's format was transfiormed to .pdb. pdbqt, 'q' denotes the addition of Kollman charges, and 't' signifies the removal of hetero atom . The Pymol software was employed to visualize the protein structure, serving as the receptor for the investigated molecule. Utilizing this tool, cartoon structures of the protein were generated[14].

Table 2:-Proteins & PDB ID

Sr.no	Protein	PDB ID
1	RNA dependent /RNA polymerase	**6M71**
2	Nucleocapsid/phosphoprotein	**6VYO**
3	Spike glycoprotein	**6VYB**
4	Spike protein ACE2	**6Y2F**

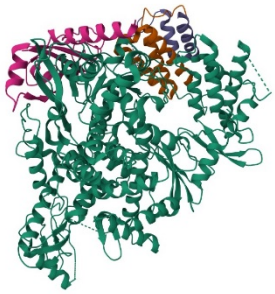

Figure 4:- 6M71

Figure 5:-6VYB

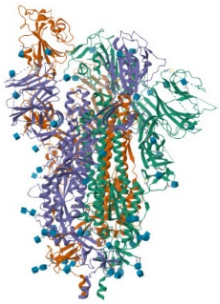

Figure 6:- 6VYO

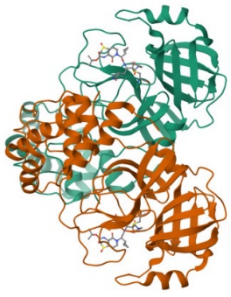

Figure 7:- 6Y2F

3)Docking Procedure:-

The PyRx tool, a comprehensive open-source platform that unifies Autodock 4, Autodock Vina, and Auto Wizard into a single environment, was used for docking investigations. The capacity of PyRx to effectively expedite the docking process for several ligands makes it stand out. PyRx does away with the necessity for prompt command knowledge, in contrast to Autodock

Vina. PyRx also includes Open Babel, a useful tool for optimising ligand molecule SDF files and converting them to the appropriate.pdb format that is compatible with the receptor molecule. Moreover, PyRx provides the ease of doing energy minimization for every chosen ligand at the same time, which helps find stable molecular conformations [15].

Result & discussion:-

1.Ramchandran plot :-

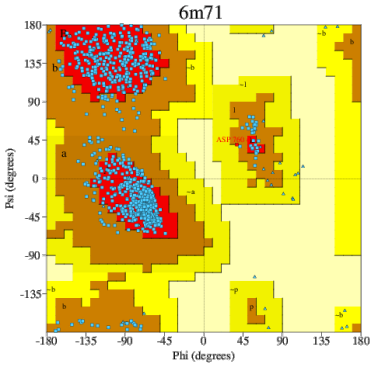

Figure 8:- 6M71

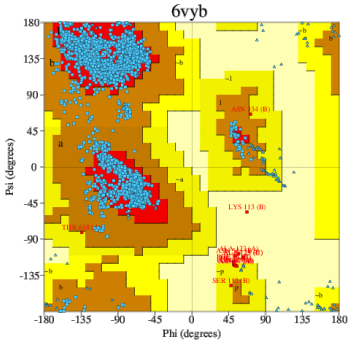

Figure 9:-6VYB

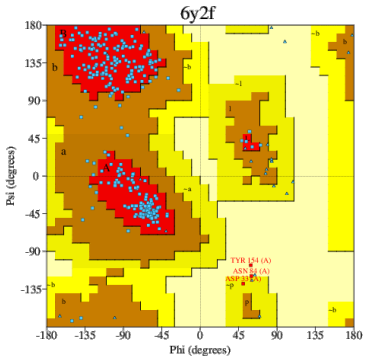

Figure 10:-6Y2F

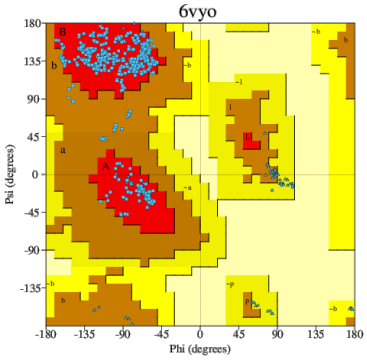

Figure 11:-6VYO

2.Ligand binding preparation:-

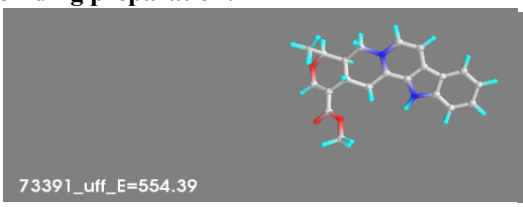

Figure 12 :-6M71& serpentine

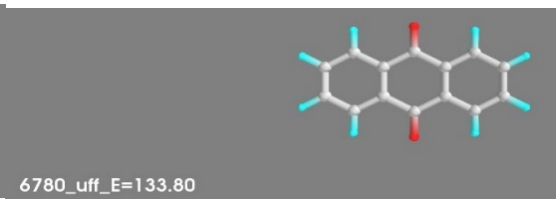

Figure 12:- 6M71&sitogluside

Figure13:- 6M71&anthraquinone

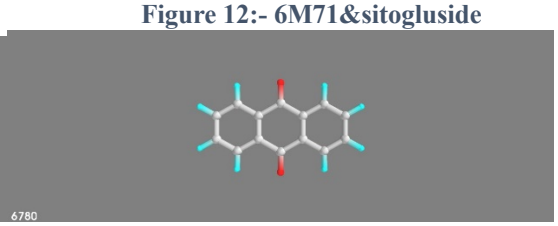

Figure 14:- 6Y2F & Sitogluside

3.Parameter gride and docking simulation:-

The molecular docking was performed to identify receptor ligand interaction. The Anthraquinone , sitogluside , serpentine were used for docking with Moringa oleifera .The grid map was created using AutoGrid and a grid box with a docking box. A grid box measuring 60 × 60 × 60 Å was used to establish the docking coordinates for TRα and 60 × 60 × 60 Å for TRβ. Box spacing measured 0.375 Å. Lastly, AutoDock was executed with a maximum of 27,000 generations and 10,000 retries. Local search in combination with a genetic algorithm was used to determine the docking options. The stimulation for each Moringa oleifera was

made up of 1000 docking runs with the default AutoDock settings.
Using AutoDock 4 and AutoDock Vina as docking tools, molecular docking was carried out. A blind docking technique was used to include every potential binding site for the ligands. The binding free energy (kcal/mol) was used to express the binding affinity[16].

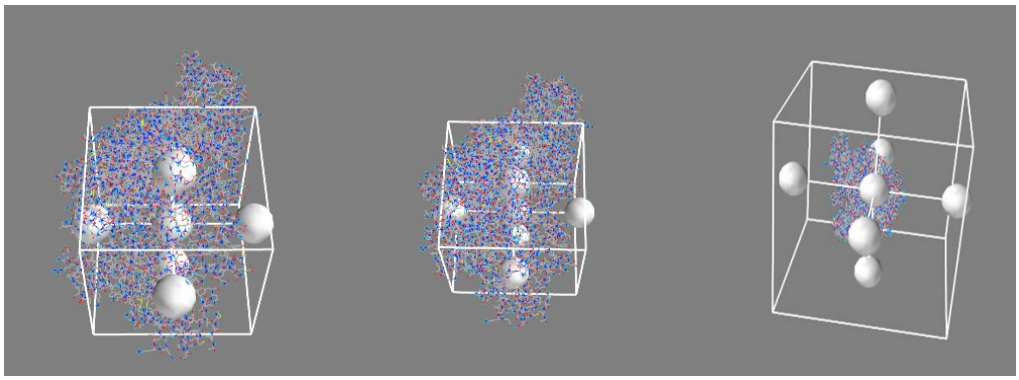

Figure 15:- 6M71& anthraquinone Figure 16:- 6M71& Sitogluside Figure 17:- 6M71 & serpentine

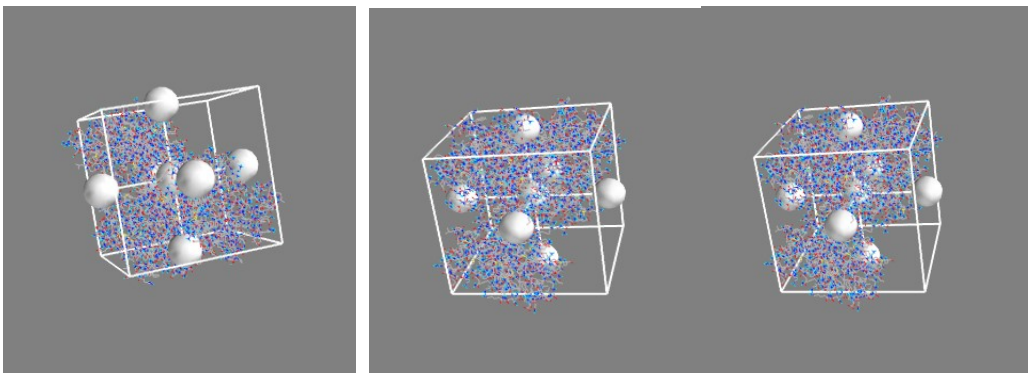

Figure 18:- 6VYB& Anthraquinone Figure 19:- 6VYB & Serpentine Figure 20:- 6VYB & Sitogluside

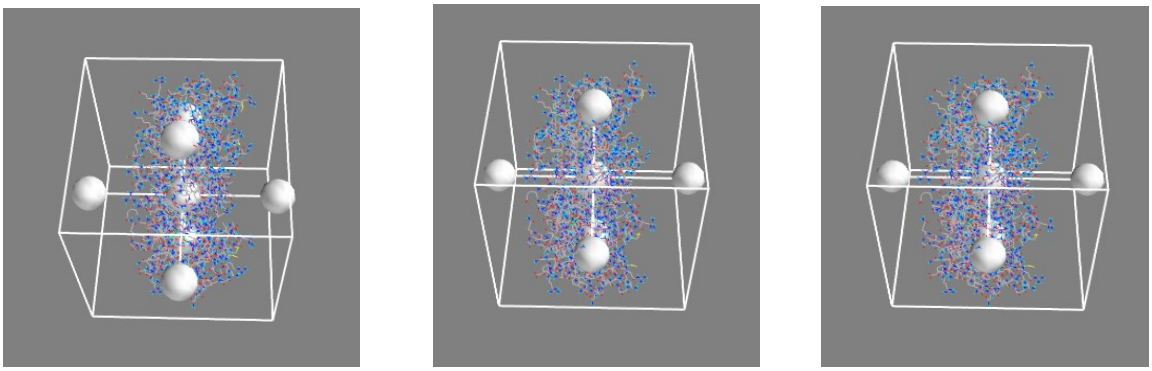

Figure 21:- 6VYO & anthraquinone Figure 22:- 6VYO & Serpentine Figure 23:- 6VYO & Sitogluside

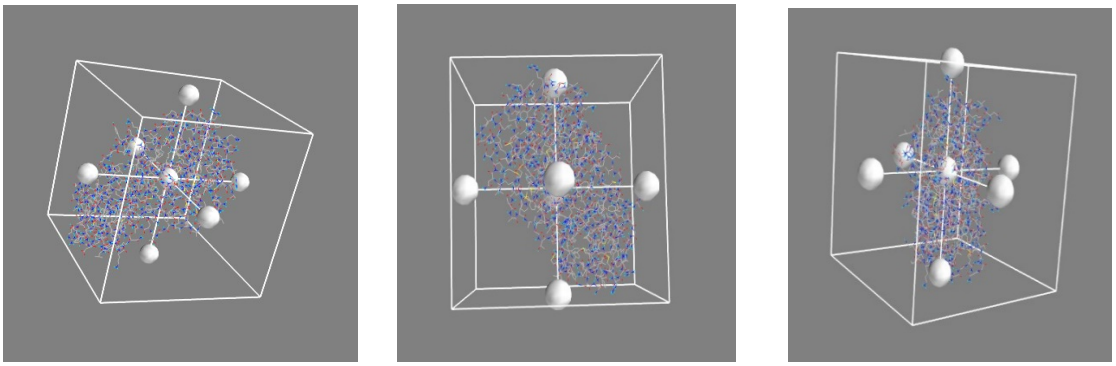

Figure 24:- 6Y2F & anthraquinone Figure 25:- 6Y2F & Sitogluside Figure 26:- 6Y2F & Serpentine

4. Binding results:-

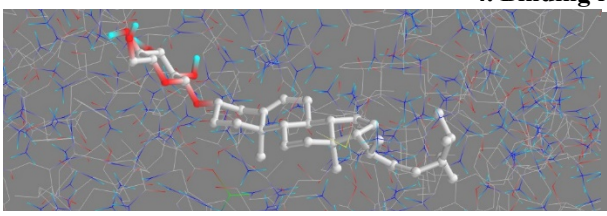

Figure 27:-6M71 & anthraquinone

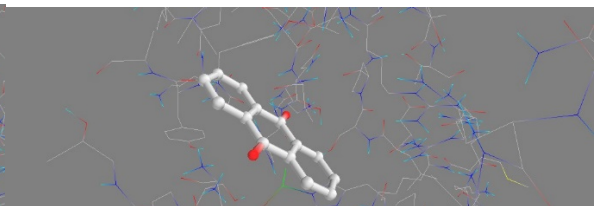

Figure 28:- 6M71& sitogluside

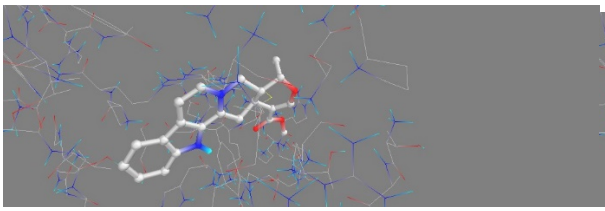

Figure 29:- 6M71 & serpentine

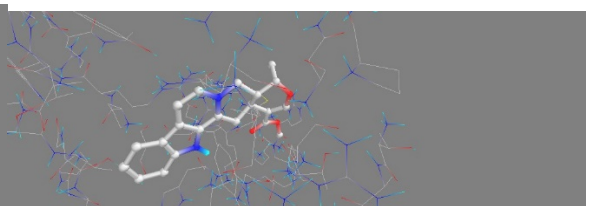

Figure 30:-6VYB & Serpentine

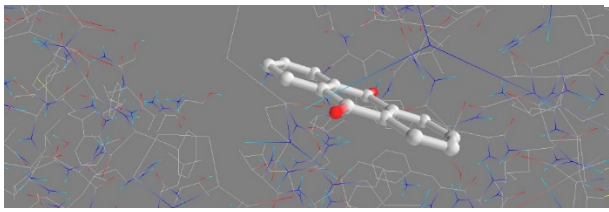

Figure 31:- 6VYB & sitogluside

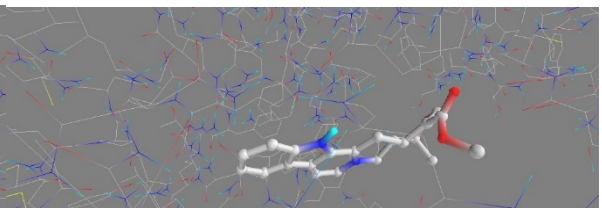

Figure 32:-6VYB & anthraquinone

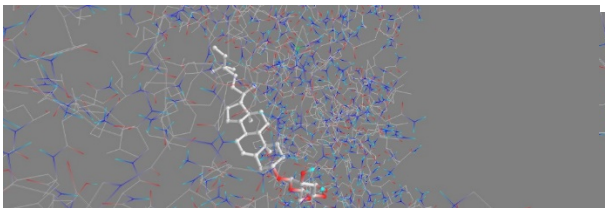

Figure 33:- 6VYO& anthraquinone

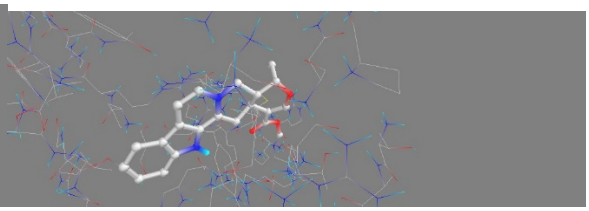

Figure 34:- 6VYO& Serpentine

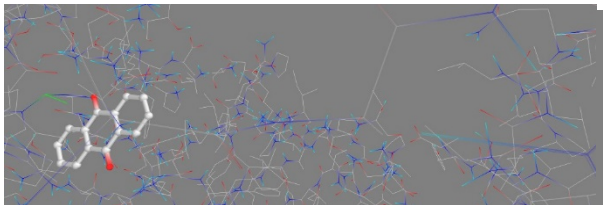

Figure 35:- 6VYO & sitogluside

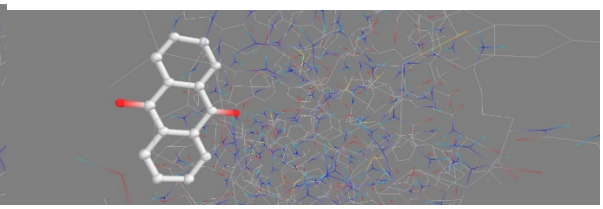

Figure 36:-6Y2F & Sitogluside

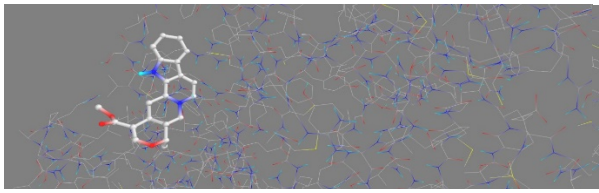

Figure 37:- 6Y2F & Serpentine

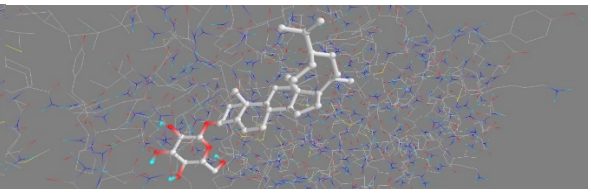

Figure 38:- 6Y2F & anthraquinone

5 Biodiscovery Discovery Docking :-

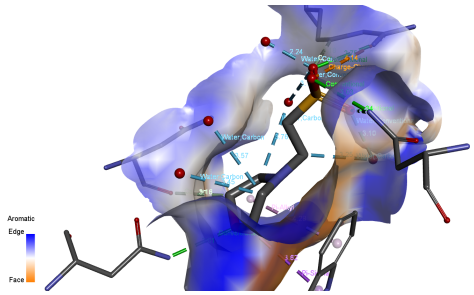

Figure 39:-Sitogluside & 6VYO

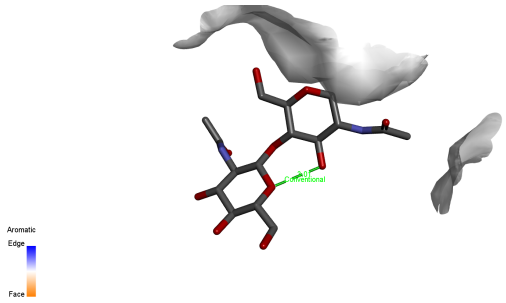

Figure 40:- Sitogluside & 6VYB

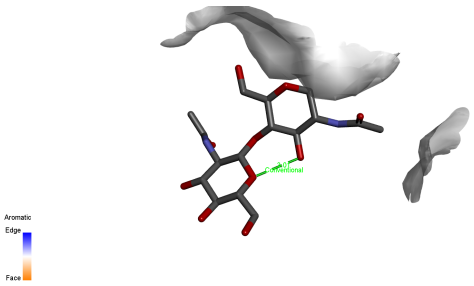

Figure 41:-Anthraquinone&6VYB

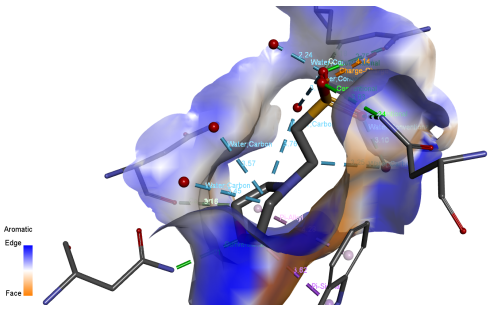

Figure 42:- Anthraquinone&6VYO

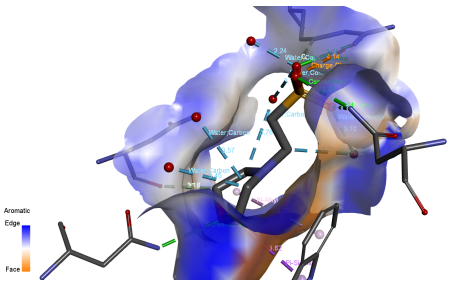

Figure 43:- Serpentine& 6VYO

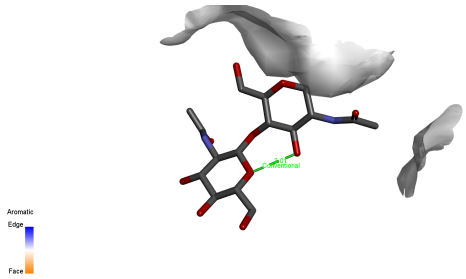

Figure 44:-Serpentine &6VYB

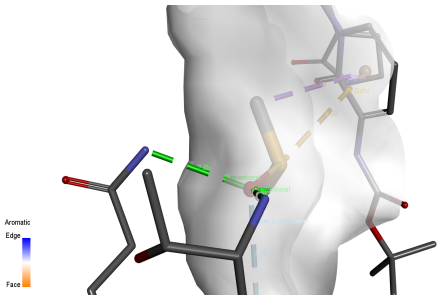

Figure 45:- Anthraquinone& 6Y2F

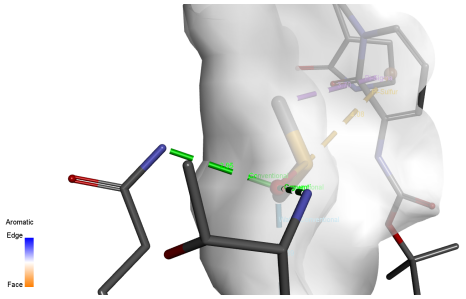

Figure 46:- Serpentine& 6Y2F

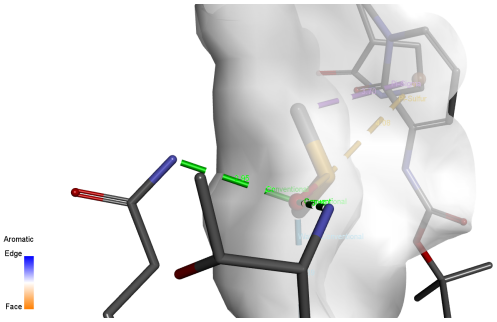

Figure 47:- Sitogluside & 6Y2F

6.Amino acid (2D Structure):-

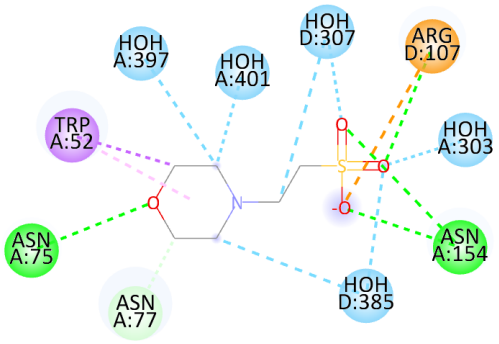

Figure 48:- anthraquinone & 6M71

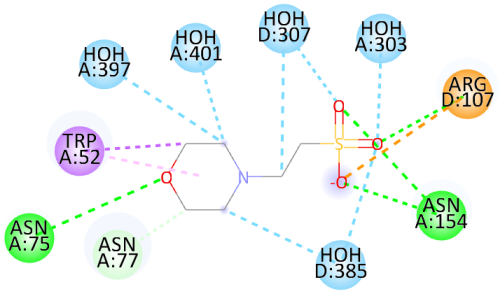

Figure 49:- Serpentine & 6VYO

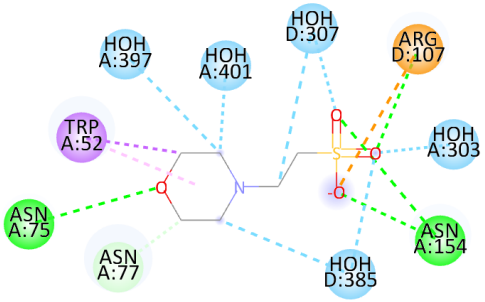

Figure 50:- Sitogluside & 6VYO

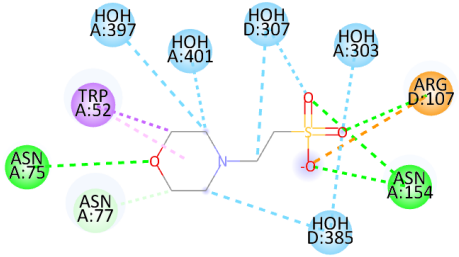

Figure 51:- Anthraquinone & 6VYO

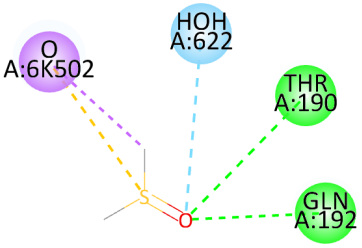

Figure 52:-anthraquinone&6Y2F

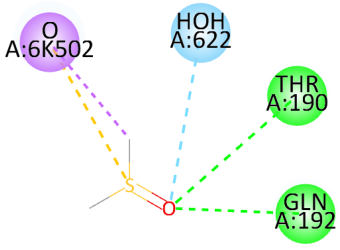

Figure 53:- Serpentine& 6Y2F

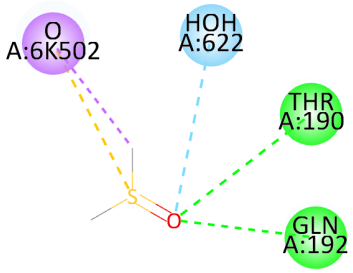

Figure 54:- Sitogluside & 6Y2F

7.Binding energy:-

Table 3:- Binding energy's of Protein & Receptors .

Sr.no	Receptors\ Protein	6M71	6VYO	6VYB	6Y2F
1	Anthraquinone	-7.4	-7.8	-7.7	-8.3
2	Sitogluside	-7.8	-7.1	-8.4	-7.3
3	Serpentine	-7.2	-7.6	-6.8	-7.5

Our model is based on the ligand based pharmacophoric features of already known active compounds of the plant species. Structures of health beneficial phytochemicals i.e. Anthraquinone, Serpentine, Sitogluside, present in M. oleifera were extracted and analyzed using PubChem & the proteins are downloaded usingn protein dada bank (PDB) & that is PDBID (6M71, 6VYB, 6VYO ,6Y2F) They have good binding energy .

Medicinal plants may treat a variety of ailments. M. oleifera is a valuable medicinal plant that has traditionally been used to treat numerous health conditions, including type 2 diabetes & covid 19 . It is mostly used in covid situation because they have good energy boost property .It is also called as energy booster

Conclusion: -

In silico molecular docking studies of M. oleifera revealed potential phytochemical targets, including anthraquinone, sitogluside ,Serpentine phytochemical classes and structural manifolds. These phytochemicals are likely to target proteins of covid 19 disease or corona virus[17]. This work suggests that M. oleifera, a polyphenolic molecule, may have antiviral properties against the COVID receptors responsible for SARS-CoV-2 illness, as anticipated in silico. Molecular docking data indicates that Anthraquinone (-7.4, -7.8, -7.7,-8.3Kcal/mol.) and Sitogluside(-7.4, -7.1, -8.4,-7.3 Kcal/mol) have higher activity than Serpentine (-7.2, -7.6, -6.8,-7.5 Kcal/mol)The polyphenolic molecule binds accurately to the receptor's active site, which is determined by the amino acids present. This study investigated pharmacokinetic characteristics and drug-likeness, identifying three molecules as potential lead compounds for future investigation[18].

Anthraquinone have maximum binding (-8.3Kcal/mol) against 6Y2F receptor , Sitogluside having maximum binding energy (-8.4Kcal /mol) against 6VYB & the Serpentine have maximum binding energy (-7.6Kcal/mol). Then In silico screening of bioactive compounds derived from *Moringa oleifera* Against SARS-CoV-2 the 6VYB was found to be the best Protein for COVID from all the selected phytoconstituent.

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